

REVIEW

Septic Cavernous Sinus Thrombosis: Case Report and Review of the Literature

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ABSTRACT

Septic cavernous sinus thrombosis is a rare but serious complication of infection of the cavernous sinuses. There are no randomised, controlled trials of management of this condition and existing reviews of the literature are somewhat dated. The authors report a case with a favourable outcome and then present the findings of a literature review of the management of this condition. Outcome data suggest that corticosteroids are of equivocal benefit whereas antibiotics and anticoagulation are beneficial.

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KEYWORDS

Cavernous sinus thrombosis; infection; treatment

Introduction

Septic cavernous sinus thrombosis is a rare but serious complication of infection of the cavernous sinuses. In the pre-antibiotic era, it was associated with high mortality rates.¹ With the introduction and widespread use of antibiotics, the outlook of this condition has improved somewhat, but this continues to depend on timely diagnosis and initiation of appropriate treatment. Potential therapies include antibiotics, corticosteroids, and anticoagulation, as well as surgical intervention for source control of the infection.² Unfortunately, there are no randomised controlled trials of any of these treatments in this condition, and so management remains somewhat ad hoc.

A number of factors need to be considered when managing these patients. These include the source of infection (if known), the likely causative organism(s) and therefore the most appropriate choice of antibiotics, the presence of any underlying medical condition(s), and whether or not surgical treatment is appropriate. We report the case of a patient with septic cavernous sinus thrombosis who eventually had a favourable outcome. We then report a review of the existing literature regarding treatment of this condition.

Case history

A 41-year-old man of Indian origin presented to a tertiary-care centre with a 1-day history of fever,

headache, and bilateral periorbital and mid-facial swelling. The day prior to the onset of his symptoms, he had attempted to burst a furuncle in the inner margin of his right nostril. He had no relevant medical history and was not on any medications. He had last travelled to India 4 months earlier.

On examination, he was conscious and alert, but was febrile (38.1°C). He had marked facial and periorbital swelling with bilateral blepharoptosis, chemosis, and proptosis. His cardiovascular and respiratory examination was normal, and there were no other neurological deficits.

On neuro-ophthalmological examination, he had a visual acuity of 6/12 bilaterally. There were no visual field defects to confrontation. Colour vision was normal, there was no relative afferent pupillary defect, and the intraocular pressures were normal. On funduscopy, there was no evidence of optic disc swelling. He had a full range of eye movements but complained of pain on moving his eyes. The conclusion was that there was no clinical evidence of optic nerve compression.

At presentation, blood cultures were taken along with swabs from the nasal furuncle. His inflammatory markers were markedly raised (white cell count 16×10^9 /L, erythrocyte sedimentation rate 67 mm/h, C-reactive protein 325 mg/L), with normal renal functions and slightly deranged liver functions tests (total bilirubin 28 μ mol/L, alkaline phosphatase 177 U/L, γ -

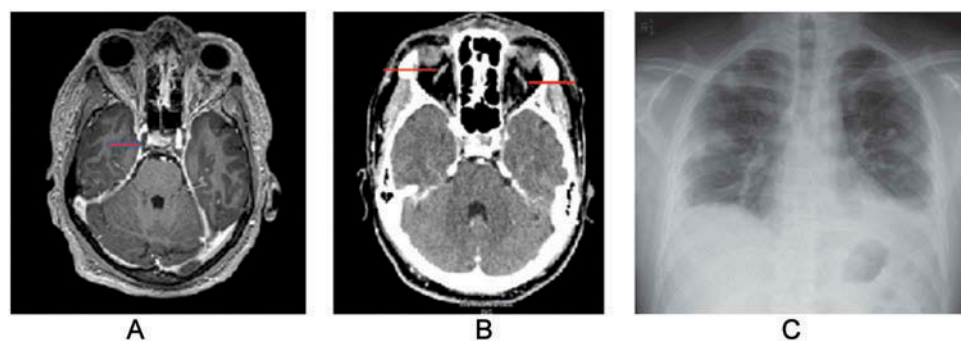


Figure 1. (A) Brain MRI (T1-weighted with gadolinium) showing non-opacification of the right cavernous sinus. (B) Contrast-enhanced brain CT showing bilateral engorged thrombosed superior ophthalmic veins. (C) Chest X ray showing multiple opacities in the lungs and left-sided pleural effusion.

glutamyltransferase 177 U/L). Tests for vasculitis, thrombophilia, human immunodeficiency virus (HIV), and diabetes were negative. Computed tomography (CT) brain (pre- and post-contrast with arteriogram and venogram) and magnetic resonance imaging (MRI)/MR venogram revealed engorged, thrombosed superior ophthalmic veins bilaterally with non-opacification of the cavernous sinuses, consistent with bilateral cavernous sinus thrombosis (Figure 1A and B).

Pending blood cultures, he was treated empirically with high-dose intravenous (IV) flucloxacillin and ceftriaxone, and was anticoagulated with enoxaparin. He was not treated with corticosteroids. Although his ophthalmological symptoms improved on the above regimen and his peri-orbital swelling subsided, 1 week after admission, he developed a cough, shortness of breath, and reduced O₂ saturation. He was transferred to the intensive care unit (ICU) at this stage. A chest X-ray revealed bilateral, multilobar consolidation with a left-sided pleural effusion (Figure 1C). Multiple blood cultures as well as cultures taken from the nasal furuncle grew methicillin-sensitive *Staphylococcus aureus* (MSSA). There was a suggestion on his echocardiogram of possible tricuspid valve vegetations. Unfortunately, he continued to deteriorate with worsening respiratory distress and was intubated. His antibiotics were changed to meropenem and linezolid because of a suspicion of a hospital-acquired pneumonia. Following this he began to improve, and his symptoms resolved over the next 2 weeks. He was discharged 1 month later on warfarin, the plan being to discontinue this after 3 months if a follow-up CT venogram showed resolution of the

thromboses. Intravenous flucloxacillin was continued for 6 weeks, followed by oral dicloxacillin. He ultimately made a full recovery.

Comment

The sequence of events that led to the admission to the ICU was felt to be as follows: venous blood carried the MSSA from his nose to his cavernous sinuses, resulting in septic cavernous sinus thrombosis. Haematogenous spread of the infection, either directly from the furuncle or from the cavernous sinuses seeded vegetations on the tricuspid valve, which, in turn, caused a shower of septic emboli to his lungs and multilobar consolidation. There was a suspicion of a hospital-acquired pneumonia complicating the above situation given the suboptimal response to the initial antibiotics. During the management of his illness, we became aware of the lack of evidence on which to base decisions regarding the use of corticosteroids and whether or not he should be anticoagulated.

Materials and methods

A literature search was carried out looking for all relevant articles published in English between January 1980 and July 2015. 1980 was chosen because imaging (CT or MRI) was more likely to be involved in making the diagnosis. The databases searched were PubMed, Embase, MEDLINE, CINAHL (EBSCO), Health & Medical Complete (ProQuest), and Health Management (ProQuest). The keywords used were

“septic”, “cavernous sinus thromboses”, “infection”, “adult”, “treatment”, and “management”.

Data extracted for each case included age, gender, source of infection, organism(s), co-morbidities, imaging modality used, details of any surgery performed, use of antibiotics, corticosteroids, use of anticoagulation, and outcome.

Results

The initial search yielded 133 articles. Paediatric cases (age <16 years) and cases of post-traumatic cavernous sinus thrombosis (CST), post-surgical CST, and CST associated with widespread cerebral venous sinus thrombosis secondary to causes such as thrombophilia were excluded. Articles reporting imaging without clinical details or clinical diagnosis without imaging confirmation were also excluded. Ultimately, 68 relevant articles were identified and all were retrieved. These included four literature reviews (1986, 1988, 1988, and 2002)^{1–4} and 64 other articles^{5–68} containing a total of 88 case reports. In the early reports from the 1980s, the diagnosis was confirmed angiographically in some patients, but most patients were diagnosed clinically and/or through post-mortem studies.¹

Of the 88 reported cases, two thirds (58 cases) were male and one third (30 cases) were female. Ages ranged from 16 to 79 years. Thirty patients (34%) had prior medical conditions that could have resulted in immunosuppression such as diabetes, chronic alcohol abuse, long-term corticosteroid use, and bone marrow transplant. Details of individual cases are provided in Table 1.

Source of infection

Not surprisingly, infections arose from anatomical sites known to drain to the cavernous sinuses. The commonest source was spread from paranasal sinusitis, accounting for 57% of patients. This included spread from maxillary, ethmoidal, and sphenoidal sinuses, with the sphenoidal sinus being the most common. Mid-facial infections (as in our patient) and dental infections were responsible for 12 and 11 cases, respectively. Incision and drainage of nasal and other facial abscesses by “untrained hands” preceded most of these cases. Otitis media and spread from distant sites

(intravenous drug use, myiasis of the eyelid, and anorectal abscess) were responsible for 3 cases each. The source was not known or not reported in 9 cases.

Causative organisms

Both bacteria and fungi were implicated (Table 2). Although blood cultures were routinely performed, isolating an organism was not always successful, often because antibiotics had been administered prior to obtaining the blood cultures and the fastidious nature of the organism involved. The commonest reported organism was methicillin-resistant *Staphylococcus aureus* (MRSA), followed by MSSA. Various streptococci, other staphylococci, oral anaerobic flora, and gram-negative organisms were also reported. *Aspergillus fumigatus* was the commonest fungal infection. Fungal infections were more commonly reported in immunocompromised patients, including patients with diabetes mellitus, connective tissue disorders, haematological malignancies, those treated with immunosuppressants, or patients who had had a bone marrow transplant. Prognosis was poor in this immunocompromised patient population irrespective of the organism, but more so when the organism was a fungus.

Imaging

The commonest imaging modality was MRI (42%), followed by contrast-enhanced CT brain (23%). The choice of modality mostly reflected the availability in different centres. In 7 case reports, the imaging modality was not mentioned, although confirmation of CST was apparently obtained through imaging.

Antibiotic use

The choice of antibiotic or antifungal depended on the organism isolated. Almost all major groups of antibiotics were used (Table 3). The commonest empirically used antibiotics were flu-cloxacillin, vancomycin, and third-generation cephalosporins. In most case studies, antibiotics were changed once an organism had been isolated, the eventual choice depending somewhat on local antibiotic guidelines and availability. Amphotericin B was the commonest antifungal

Table 1. Demographics, treatment, and outcome of cases with septic cavernous sinus thrombosis.

Reference	Case	Age/Sex	Co-morbidities/ Immunocompromised		Organism(s)	Antibiotics	Surgery	Anticoagulation	Corticosteroid use	Outcome
			Source	No						
5	1	18/M	Sphenoid sinusitis	No	<i>Bacteroides, Streptococcus intermedius</i> , mixed anaerobes	Narrow-spectrum penicillin, chloramphenicol, Aminoglycoside	Trans-septal sphenoidotomy	Not used	Yes—high-dose steroids for retinal congestion and early papilloedema	Full recovery
6	2	18/M	Maxillary, ethmoid, sphenoid sinusitis	N/A	<i>Peptostreptococcus anaerobius, Fusobacterium nucleatum</i>	N/A	N/A	N/A	N/A	Death
7	3	32/M	Ethmoid and sphenoid sinusitis	N/A	Gram-negative bacilli	N/A	Drainage of periorbital abscess and ICA aneurysm repair	N/A	No	Full recovery
8	4	73/M	Sphenoid sinusitis	Diabetes, 6 months of steroids for temporal arteritis, hypertension, coronary artery disease	<i>Aspergillus fumigatus</i>	Amphotericin B	Right sphenoidotomy	N/A	No	Death
9	5	67/M	Left otitis media	N/A	Group A β -haemolytic streptococci	Narrow-spectrum penicillin, metronidazole	N/A	No—but APTT-61	N/A	Survived—blind
10	6	60/M	Dental abscess	Diabetes	<i>Pseudomonas aeruginosa, Enterococcus</i>	Broad-spectrum penicillin, aminoglycoside, vancomycin	I&D of buccal and periauricular region abscess	IV heparin	N/A	Survived
11	7	19/M	Bilateral purulent otitis media	N/A	<i>Pseudomonas aeruginosa, coagulase-negative staphylococci</i> MRSA	Vancomycin, aztreonam, broad-spectrum penicillin, aminoglycoside	Left mastoidectomy, intranasal sphenoidotomy, incision of the sigmoid sinus, and clot retrieval	IV heparin post op changed to warfarin for total 3 months	N/A	Full recovery
12	8	23/F	Facial furuncle nose	Post-partum		Chloramphenicol, narrow-spectrum penicillin, vancomycin	N/A	IV heparin	N/A	Full recovery
13	10	49/M	Sphenoid sinusitis	Diabetes	<i>Pseudomonas aeruginosa, Staphylococcus aureus</i>	Vancomycin, 3rd G cephalosporin, fluoroquinolones	N/A	N/A	N/A	Survived
14	9	26/M	Pan sinusitis	No	α -Haemolytic streptococcus, coagulase-negative staphylococci	3rd G cephalosporin, vancomycin, metronidazole	Drainage of ethmoid and maxillary sinuses and evacuation of the subdural empyema	N/A	Yes	Survived with a blind right eye and pituitary insufficiency
15	13	69/M	Dental abscess	N/A	Diphtheroid, <i>Pseudomonas aeruginosa</i>	Narrow-spectrum penicillin, 3rd G cephalosporin, metronidazole	Tracheotomy, I&D of the parapharyngeal abscess, extraction of the right third molar	IV heparin, then warfarin	N/A	Full recovery

(Continued)

Table 1. (Continued).

Reference	Case	Age/Sex	Source	Co-morbidities/ Immunocompromised	Organism(s)	Antibiotics	Surgery	Anticoagulation	Corticosteroid use	Outcome
16	14	32/F	Sphenoid and ethmoid sinusitis	Systemic lupus erythematosus on high-dose steroid and cyclophosphamide	<i>Pseudomonas aeruginosa</i>	3rd G cephalosporin, aminoglycoside	N/A	N/A	Hydrocortisone physiological replacement	Death
17	11	50/M	Nasal furuncle	Diabetes	<i>Proteus mirabilis</i> , <i>Staphylococcus aureus</i>	Narrow-spectrum penicillin, metronidazole, aminoglycoside	Superior orbitotomy	N/A	N/A	Full recovery
18	12	38/M	Sinusitis	N/A	<i>Pseudomonas aeruginosa</i>	Vancomycin, 3rd G cephalosporin	Medial orbitotomy with ethmoidectomy and maxillary antrostomy	N/A	N/A	Full recovery
19	15	36/M	Ethmoid sinusitis	Bone marrow transplant	Zygomycetes	Amphotericin B	No	No	No	Death
20	16	30/M	Unknown	No	MRSA	Vancomycin	N/A	N/A	N/A	Full recovery
21	17	53/F	Pan sinusitis	Systemic lupus erythematosus (SLE)	Mucormycosis	Amphotericin B	N/A	N/A	Yes but for treatment of SLE	Death
22	18	20/M	Pan sinusitis	No	<i>Streptococcus</i> group C	3rd G cephalosporin narrow-spectrum penicillin	Endoscopic sinus surgery and I&D of orbital abscess	IV heparin and then warfarin	Dexamethasone added post surgery after a few days to reduce sinus inflammation	Full recovery
23	19	17/F	Ethmoid and sphenoid sinusitis	No	<i>Streptococcus milleri</i>	3rd G cephalosporin, vancomycin, metronidazole, carbapenem	Endoscopic drainage of the right sphenoid and ethmoid sinuses and operative drainage of left eye abscess	IV heparin and then warfarin	N/A	Survived—rehab
24	20	39/M	Sphenoid sinusitis	Chronic alcohol consumption	<i>Streptococcus constellatus</i>	Narrow-spectrum penicillin	N/A	N/A	N/A	Full recovery
25	21	19/M	Pan sinusitis	N/A	No pathogen isolated	N/A	Yes	N/A	N/A	Survived
26	22	37/M	Sphenoid and ethmoid sinusitis	Bone marrow transplant	<i>Aspergillus</i> species unsure	Amphotericin B	No	IV heparin	No	Death
27	23	55/F	Periodontal disease	No	<i>Fusobacterium nucleatum</i> , α -haemolytic streptococci	Vancomycin, 3rd G cephalosporin, clindamycin	Bifrontal craniotomy and decompression of the left optic nerve	No	Yes—not mentioned	Survived—blind
28	24	35/F	IVDU	Intravenous drug use	MRSA	3rd G cephalosporin, metronidazole, narrow-spectrum penicillin, vancomycin, rifampicin	N/A	Dalteparin (LMW heparin) changed to IV heparin	IV hydrocortisone	Death
29	25	68/F	Ethmoid and sphenoid sinusitis	No	<i>Aspergillus fumigatus</i> , non-invasive	3rd G cephalosporin, fluoroquinolone	Bilateral video-assisted sphenoidotomy	IV heparin	Prednisolone	Full recovery

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Table 1. (Continued).

Reference	Case	Age/Sex	Source	Co-morbidities/ Immunocompromised	Organism(s)	Antibiotics	Surgery	Anticoagulation	Corticosteroid use	Outcome
26	56/F	Sphenoid sinusitis	No	<i>Aspergillus fumigatus</i> , non-invasive	3rd G cephalosporin, fluoroquinolone, broad-spectrum penicillin	Video-assisted bilateral sphenoidotomy	IV heparin followed by warfarin for 6 months	N/A	Full recovery	
27	50/M	Maxillary sinusitis	Diabetes	Mucormycosis	Amphotericin B	Resection of nasal debris	N/A	N/A	Full recovery	
28	72/F	Following antral lavage	N/A	<i>Aspergillus</i> species	Amphotericin B	Enucleation of eye and trans-nasal débridement	N/A	N/A	Full recovery	
29	63/F	Maxillary and sphenoid sinusitis	No	<i>Fusobacterium nucleatum</i>	Narrow-spectrum penicillin, chloramphenicol	N/A	N/A	Yes	Survived with hemiparesis	
30	62/M	Paranasal sinusitis	Diabetes	Zygomycete	N/A	Yes	N/A	N/A	Death	
31	45/M	Paranasal sinusitis	Bone marrow transplant	<i>Staphylococcus simulans</i>	N/A	N/A	N/A	N/A	Survived—no vision in left eye	
32	16/F	Paranasal sinusitis	Acute myeloid leukaemia	N/A	N/A	N/A	N/A	N/A	Death	
33	71/M	Paranasal sinusitis	Diabetes	Fungus—type not mentioned	Amphotericin B	Yes	N/A	N/A	Survived	
34	57/M	Paranasal sinusitis	Asthma	<i>Peptostreptococcus micros</i>	N/A	N/A	N/A	N/A	Survived	
35	59/M	Paranasal sinusitis	Diabetes	Zygomycete	N/A	N/A	N/A	N/A	Death	
36	76/M	Paranasal sinusitis	Chronic myeloproliferative disorder	Zygomycete	Amphotericin B	N/A	N/A	N/A	Death	
37	79/M	Paranasal sinusitis	Diabetes	<i>Streptococcus constellatus</i>	N/A	N/A	N/A	N/A	Survived	
38	62/F	Paranasal sinusitis	Diabetes	<i>Aspergillus</i>	Amphotericin B, voriconazole	Yes	N/A	N/A	Survived	
39	65/F	Sphenoid sinusitis	Diabetes, hypertension, hyperlipidaemia	N/A	4th G cephalosporin	Drainage of sphenoid sinus	No	N/A	Death	
40	55/M	Dental infection	No	<i>Streptococcus anginosus</i>	Vancomycin, 3rd G cephalosporin, metronidazole, narrow-spectrum penicillin	N/A	Tinzaparin s/c daily for 2 weeks	N/A	Full recovery	
43	56/F	N/A	No	<i>Streptococcus constellatus</i>	Broad-spectrum penicillin	No	No	No	Survived	
41	31/F	Sphenoid sinusitis	No	<i>Haemophilus influenzae</i>	Narrow-spectrum penicillin, vancomycin, 3rd G cephalosporin	Bilateral sphenoidotomies with evacuation of the sinuses	No	N/A	Full recovery	
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Table 1. (Continued).

Reference	Case	Age/Sex	Source	Co-morbidities/ Immunocompromised		Organism(s)	Antibiotics	Surgery	Anticoagulation	Corticosteroid use	Outcome
36	42	27/M	Concrete shrapnel injury to nostril	No	MRSA	Vancomycin, rifampicin, cotrimoxazole, linezolid	No	IV heparin changed to enoxaparin and continued for 6 weeks	N/A	Full recovery	
	44	24/M	Expression of facial abscess by GP	No	N/A	N/A	Bilateral ethmoidectomies and antral washings	N/A	N/A	Survived—rehab	
	45	22/F	I&D of facial abscess by GP	No	N/A	N/A	N/A	N/A	N/A	Full recovery	
37	46	49/M	Sphenoid and ethmoid sinusitis	Hypertension, recurrent rhinosinusitis	<i>Aspergillus fumigatus</i> , <i>Staphylococcus</i>	Vancomycin, voriconazole, broad-spectrum penicillin	Endoscopic anterior and posterior ethmoidectomies, uncinectomy and left sphenoidotomy	IV heparin followed by warfarin	N/A	Full recovery	
	38	47	34/M	Maxillary, sphenoid and ethmoid sinusitis	No	MRSA	Vancomycin, aminoglycoside, rifampicin, daptomycin	Surgical drainage of the sinuses	N/A	Death	
39	48	44/M	Pustule in naris	No	MRSA	Vancomycin, trimethoprim–sulfamethoxazole, rifampicin, metronidazole, 3rd G cephalosporin	N/A	N/A	N/A	Survived—blind	
	49	67/M	Unknown	N/A	<i>Porphyromonas gingivalis</i>	Broad-spectrum penicillin, carbapenem	Lateral orbital osteotomy and drainage of the abscess	N/A	Methyl prednisolone given initially as suspected inflammatory lesion	Full recovery	
41	50	60/M	Branding of the temple and vertex by a faith healer	Glaucoma	N/A	Broad-spectrum penicillin, 3rd G cephalosporin	N/A	N/A	N/A	Survived—blind	
	51	64/F	Paranasal sinusitis	Hypertension	N/A	Broad-spectrum penicillin	Yes	IV heparin	N/A	Survived	
	42	52	67/M	Unknown	N/A	MRSA	N/A	N/A	N/A	Survived	
43	53	62/F	Periodontitis	Hypertension	<i>Gram-negative coccobacilli</i> , <i>Fusobacterium</i>	Amphotericin B, 2nd G cephalosporin, 3rd G metronidazole	Trans-arterial embolization	IV heparin	N/A	Full recovery	

(Continued)



Table 1. (Continued).

Reference	Case	Age/Sex	Source	Co-morbidities/ Immunocompromised	Organism(s)	Antibiotics	Surgery	Anticoagulation	Corticosteroid use	Outcome
44	54	17/M	Sinusitis	No	N/A	N/A	Drainage of sinuses	yes—type not mentioned, 6 weeks	N/A	Full recovery
45	55	19/F	Vesicular lesion in tip of nose	No	MRSA	Vancomycin, 3rd G cephalosporin, broad-spectrum penicillin	N/A	IV heparin, warfarin 6 weeks	N/A	Survived—no vision in left eye
46	56	49/M	Dental infection	Chronic alcoholism	<i>Pseudomonas aeruginosa</i>	3rd G cephalosporin, clindamycin	Drainage of facial abscess	N/A	N/A	Survived
47	57	43/M	Myiasis of eye lid	Diabetes	<i>Streptococcus</i> , anaerobes	Vancomycin, 3rd G cephalosporin	N/A	N/A	N/A	Died
48	58	37/M	I&D of facial abscess	Psychosis, sickle cell trait	MSSA	Vancomycin, narrow-spectrum penicillin	N/A	IV heparin	N/A	Full recovery
49	59	49/M	Periodontitis	N/A	N/A	N/A	Extraction of teeth	N/A	N/A	Survived
50	60	45/M	Periodontitis	No	<i>Streptococcus constellatus</i>	3rd G cephalosporin, vancomycin	Extraction of teeth	s/c LMW heparin and warfarin for 3 months	N/A	Full recovery
51	61	32/F	The removal of a maxillary left third molar	No	N/A	Vancomycin, 3rd G cephalosporin, Fluconazole	I&D of abscess	IV heparin	N/A	Survived
62	77/F		Teeth extraction	N/A	N/A	N/A	N/A	Yes—type not specified	Yes for temporal arteritis	Full recovery
54	63	45/F	Sphenoid and ethmoid sinusitis	Diabetes	MSSA	Carbapenem, linezolid	Posterior ethmoidectomy and sphenoidectomy	N/A	N/A	Full recovery
55	64	61/M	Anorectal abscess	Diabetes	N/A	Broad-spectrum penicillin, fosfomycin, vancomycin	N/A	IV heparin	N/A	Survived
56	65	57/M	Maxillary sinusitis	Diabetes, coronary artery disease, hypertension	<i>Escheria coli</i> , <i>Klebsiella pneumoniae</i> , <i>Aspergillus</i>	Vancomycin, amphotericin B, carbapenem, voriconazole	Ethmoidectomy, sphenoidectomy, maxillary antrostomy, and orbital decompression	IV heparin	N/A	Died
57	66	55/M	Maxillary rhinosinusitis	Diabetes	<i>Fusarium</i>	Amphotericin B	Sinus lavage	N/A	N/A	Full recovery
58	67	N/A F	Periodontitis	Pregnant	<i>Streptococcus milleri</i>	N/A	N/A	N/A	N/A	N/A
59	68	25/M	Nasal furuncle	Treated respiratory TB, latent hepatitis-C, distant IV drug abuse	MRSA	Vancomycin, broad-spectrum penicillin, amphotericin B	N/A	IV heparin	N/A	Died
60	69	45/M	Otitis media	N/A	<i>Actinomyces naeslundii</i> , <i>Actinomyces meyeri</i>	3rd G cephalosporin, vancomycin, metronidazole	N/A	IV heparin and then warfarin for 3 months	N/A	Survived with abducens palsy

(Continued)

Table 1. (Continued).

Reference	Case	Age/Sex	Source	Co-morbidities/ Immunocompromised	Organism(s)	Antibiotics	Surgery	Anticoagulation	Corticosteroid use	Outcome
59	70	18/M	N/A	Sickle cell trait, Osgood-Schlatter disease	Group C streptococcus	3rd G cephalosporin, vancomycin, narrow- spectrum penicillin	N/A	SC heparin 5000 U tds as platelets low	Dexamethasone for orbital oedema	Full recovery
60	71	62/M	N/A	N/A	Syphilis	Narrow-spectrum penicillin	N/A	N/A	N/A	N/A
	72	50/M	N/A	N/A	Syphilis	Narrow-spectrum penicillin	N/A	N/A	N/A	N/A
61	80	63/M	N/A	No	Leptospirosis	N/A	N/A	N/A	N/A	N/A
62	73	75/F	Sphenoid sinusitis	No	<i>Streptococcus constellatus</i>	N/A	Endoscopic endonasal surgery	IV heparin for 11 days warfarin for 7 weeks	No	Full recovery
63	74	19/M	Pan sinusitis	No	<i>Streptococcus</i>	N/A	Maxillary antrostomies, total ethmoidectomies and sphenoideotomies	yes-type not mentioned	Dexamethasone for cerebral vasospasms	Survived—rehab
64	75	16/F	Impetigo in preauricular region	No	MRSA	3rd G cephalosporin, vancomycin, rifampicin	N/A	enoxaparin and warfarin at day 5 for 3 months	Dexamethasone for meningitis	Survived with residual right hemiparesis
65	76	21/M	Pan sinusitis	Diabetes	Invasive mucormycosis <i>Campylobacter rectus</i>	Amphotericin B	Débridement of sinuses	IV heparin	N/A	Died from stroke
66	77	55/M	N/A	No	N/A	Vancomycin, clindamycin, broad- spectrum penicillin	N/A	Yes—type not specified	Yes	Survived with ophthalmoplegia
67	78	65/M	Sinusitis, ethmoiditis	N/A	N/A	N/A	N/A	IV heparin	N/A	Full recovery
	79	55/M	Maxillary and ethmoid sinusitis	Diabetes	<i>Aspergillus</i>	Amphotericin B	Functional endoscopic sinus surgery	N/A	N/A	Full recovery
68	81	26/F	Sphenoid sinusitis	No	<i>Haemophilus influenzae</i>	Broad-spectrum penicillin	Endoscopic sphenoideotomy	LMW heparin for 21 days	No	Full recovery
82	37/F		Sphenoid sinusitis	No	<i>Staphylococcus aureus</i> , <i>Streptococcus species</i>	3rd G cephalosporin, metronidazole, broad- spectrum penicillin	Endoscopic sphenoideotomy	IV heparin 60 days	No	Full recovery
83	33/M		Sphenoid and ethmoid sinusitis	No	<i>Aspergillus fumigatus</i>	3rd G cephalosporin, metronidazole, broad- spectrum penicillin	Right sphenoideotomy and ethmoidectomy	LMW heparin 11 days, warfarin 45 days	No	Survived with a Horner's syndrome
84	55/M		Pan sinusitis	No	<i>Streptococcus milleri</i>	3rd G cephalosporin, metronidazole, broad- spectrum penicillin	Bilateral sphenoideotomy, right maxillary antrostomy, craniotomy for frontal empyema	IV heparin, 21 days	No	Survived—no vision in left eye

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Table 1. (Continued).

Reference	Case	Age/Sex	Source	Co-morbidities/ Immunocompromised	Organism(s)	Antibiotics	Surgery	Anticoagulation	Corticosteroid use	Outcome
85	23/F	Sphenoid and ethmoid sinusitis	No	<i>Staphylococcus aureus</i> , <i>Serratia marcescens</i>	3rd G cephalosporin, metronidazole	Sphenoidectomy and ethmoidectomy, endovascular occlusion of the right internal carotid artery	LMW heparin for 45 days	No	Full recovery	
86	26/F	Sphenoid sinusitis	No	<i>Streptococcus milleri</i>	3rd G cephalosporin, metronidazole	Bilateral sphenoidectomy, ethmoidectomy, craniotomy	LMW heparin for 30 days, warfarin 30 days	No	Full recovery	
87	50/F	Sphenoid sinusitis	No	Buccal bacterial flora, <i>Aspergillus fumigatus</i>	Broad-spectrum penicillin	Sphenoidectomy and ethmoidectomy	LMW heparin for 5 days, warfarin 30 days	No	Full recovery	
Current Case	88	41/M	Nasal furuncle	No	MSSA	No	Enoxaparin for 30 days, warfarin for 3 months	No	Full recovery	

Table 2. Organisms isolated from patients with cavernous sinus thrombosis.

Organism	Number	Percentage
Gram-positive cocci		
Coagulase-positive <i>Staphylococcus</i>		
• Methicillin-resistant <i>Staphylococcus aureus</i>	11	13
• Methicillin-sensitive <i>Staphylococcus aureus</i>	5	6
Coagulase-negative <i>Staphylococcus</i>	3	3
• <i>Staphylococcus simulans</i>	1	1
<i>Streptococcus</i>		
• α -Haemolytic streptococci	1	1
• β -Haemolytic streptococci	2	2
Group C streptococcus	2	2
<i>Enterococcus</i>	1	1
Group F streptococcus		
• <i>Streptococcus milleri</i>	4	5
• <i>Streptococcus constellatus</i>	5	6
• <i>Streptococcus anginosus</i>	1	1
<i>Peptostreptococcus</i>		
• <i>Peptostreptococcus anaerobius</i>	4	5
• <i>Peptostreptococcus micros</i>	4	5
Gram-negative bacilli		
• <i>Pseudomonas aeruginosa</i>	7	8
• <i>Fusobacterium nucleatum</i>	4	5
• <i>Haemophilus influenzae</i>	3	3
• <i>Campylobacter rectus</i>	1	1
• <i>Proteus mirabilis</i>	1	1
• <i>Klebsiella pneumoniae</i>	1	1
• <i>Serratia marcescens</i>	1	1
• <i>Escherichia coli</i>	1	1
Gram-positive bacilli		
• <i>Actinomyces naeslundii</i> and <i>meyerii</i>	1	1
Spirochaetes		
• <i>Treponema pallidum</i>	2	2
• <i>Leptospira</i>	1	1
Fungi		
• <i>Aspergillus fumigatus</i>	10	11
• Zygomycetes	4	5
• Mucorales	3	3
• <i>Fusarium</i>	1	1
Not available	13	15

Note. Totals add up to more than 100% because some cases yielded multiple organisms.

used. Most reports did not mention the duration of antibiotic use, but prolonged courses were commonly reported if seeding of other organs (such as cardiac valves or long bones) was

suspected, with fungal infection, and in immuno-compromised hosts.

Surgery

A surgical procedure was performed in 54% of patients. These were mostly on the paranasal sinuses to address the source of infection (e.g., ethmoidectomy, sphenoidectomy, maxillary antrostomy, etc.). Other procedures performed included incision and drainage of abscesses, dental extractions, craniotomy for evacuation of subdural empyema, and orbital decompression. One patient underwent an incision of the sigmoid sinus and clot retrieval with subsequent full recovery.

Corticosteroids and anticoagulation

In the previous four reviews,^{1–4} the authors attempted to address these issues but evidence was conflicting. Southwick et al.¹ looked at case reports of patients from 1940 to 1984 and concluded that mortality was lower among patients who received heparin treatment. They also concluded that corticosteroids might have a place in reducing cranial nerve dysfunction and orbital congestion. Levine et al.³ found no conclusive evidence that anticoagulation reduced mortality, although there was a non-significant trend towards benefit and there was evidence suggesting reduced residual morbidity when used early in combination with antibiotics. They did not evaluate corticosteroid use.

Of the 88 cases in our review, 15 patients received corticosteroids, but there were various reasons cited. Five patients received corticosteroids to reduce inflammation in cranial and orbital structures, one received “replacement doses” and the others received

Table 3. Antibiotics used in treating cavernous sinus thrombosis.

Class	Antibiotic	Number	Percentage
Beta-lactams	Nafcillin, amoxicillin/clavulanate, crystalline penicillin, flucloxacillin, meropenem, ticarcillin, aztreonam ampicillin/sulbactam, imipenem, piperacillin/tazobactam	37	43
Aminoglycosides	Gentamicin, tobramycin, netromycin	5	6
Cephalosporins	Cefotaxime, ceftriaxone, ceftazidime, cefpirome, cefuroxime	31	36
Fluoroquinolones	Ofloxacin	3	3
Rifamycins	Rifampicin	5	6
Miscellaneous	Chloramphenicol, metronidazole, co-trimoxazole, linezolid, daptomycin, clindamycin, fosfomycin, vancomycin	54	62
Antifungals	Amphotericin B, voriconazole, fluconazole	19	22

Note. Totals add up to more than 100% because some cases were treated with multiple antibiotics.

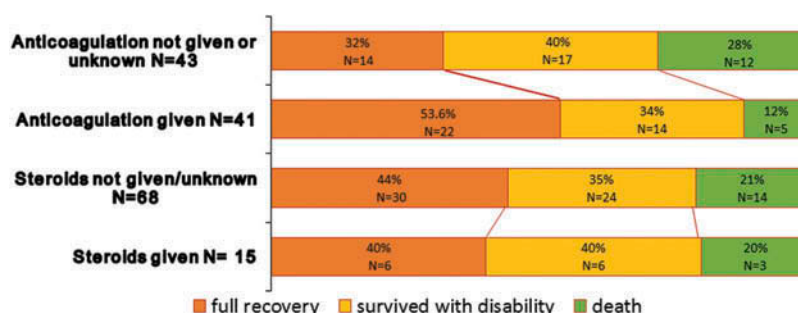


Figure 2. Patient outcome following use of steroids and anticoagulation.

corticosteroids for other indications such as treatment of concomitant systemic lupus erythematosus, meningitis, as part of a bone marrow transplant protocol, or an initial (incorrect) working diagnosis of temporal arteritis. The remainder of the patients either did not receive corticosteroids or their use was not mentioned. When comparing patients who were given corticosteroids with patients who were not given or status unknown, approximately equal percentages made a full recovery (40% vs. 44%), survived with disability (40% vs. 35%), or died (20% vs. 21%), suggesting that there was no clear overall benefit from corticosteroid use.

Anticoagulation was mentioned in the management in 41 out of 88 patients; of the remainder, one half were not treated with anticoagulants whereas their use was not mentioned in the other half. The anticoagulant most commonly used was heparin, followed by warfarin, but a few cases were treated with tinzaparin, enoxaparin, and dalteparin, and the exact agent was not specified in a few other cases. The duration of therapy was also variable, generally ranging from 2 to 6 weeks, but 5 patients received therapy for 3 months or more. Compared with patients who were not anticoagulated, a considerably greater number of anticoagulated patients made a full recovery (53.6% vs. 32%) and fewer patients died (12% vs. 28%) (see Figure 2). However, there was no clear difference in morbidity, with almost equal proportions of patients surviving with disability in each group (34% vs. 40%).

Discussion

Our literature review identified only 88 case reports of infective cavernous sinus thrombosis in the literature over a period of 25 years providing class IV evidence for the management of septic cavernous sinus

thrombosis. We acknowledge the limitations associated with a retrospective review of cases such as lack of standardised reporting across cases and the inability to control for and measure other variables that likely impacted outcomes (i.e., age, level of disability, premorbid health status, delays to treatment, etc.). There was a strong suggestion of reporting bias, with a tendency to report cases with better outcomes. Antibiotics were undoubtedly beneficial, although empirical use was variable and the ultimate choice was dependent on which organism was eventually isolated. Surgery was used for treatment of the source of infection rather than the cavernous sinus infection/thrombosis per se. There was no signal that corticosteroids were beneficial, although they might be required for other reasons. There was a strong suggestion that anticoagulation improved mortality, although there did not seem to be any benefit to morbidity. Unfortunately, evidence regarding how long to continue anticoagulation was lacking. It is clear that further studies are needed to determine the optimal therapy for this condition. These are likely to be multicentre studies in view of the rarity of the disease.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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